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BRADYKININ INDUCED EOSINOPHILIA IN "SKIN WINDOWS"

By

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Several lines of evidence indicate that kinin peptides participate in the inflammatory process (3, 7). Injected into tissue, bradykinin produces vasodilatation, increased vascular permeability, smooth muscle stimulation, and pain. The cellular response to bradykinin has been studied in tissue sections (1). With large doses there is attraction of leukocytes to the injected site. According to *Archer* (1) bradykinin has not been found chemotactic for eosinophils. In previous studies on "skin windows" (6) two of us found that histamine and histamine liberators gave rise to eosinophilia. The present paper describes the cellular response to bradykinin, as demonstrated by the skin window technique (5).

MATERIAL AND METHODS

The studies included 19 adults suffering from local skin diseases which did not involve the skin of the arms. None presented a family history of atopy. In all patients the direct eosinophil counts, the leukocyte counts and the differential counts were within normal limits. The "skin windows" were made by scraping away the epidermis from a 1×1 cm area on the volar surface of the forearm. The excoriations were covered by coverslips, which were changed at various intervals through 48 hours.

Immediately before the first coverslip was applied, each patient received an intradermal injection. Eleven patients received intradermal injections of $20 \mu\text{g}$ bradykinin in 0.2 ml aqueous solution. Four patients received $1 \mu\text{g}$ bradykinin in 0.1 ml solution and four patients $0.1 \mu\text{g}$ bradykinin in 0.1 ml solution. Eight

SKIN WINDOWS FOLLOWING INJECTION OF BRADYKININ

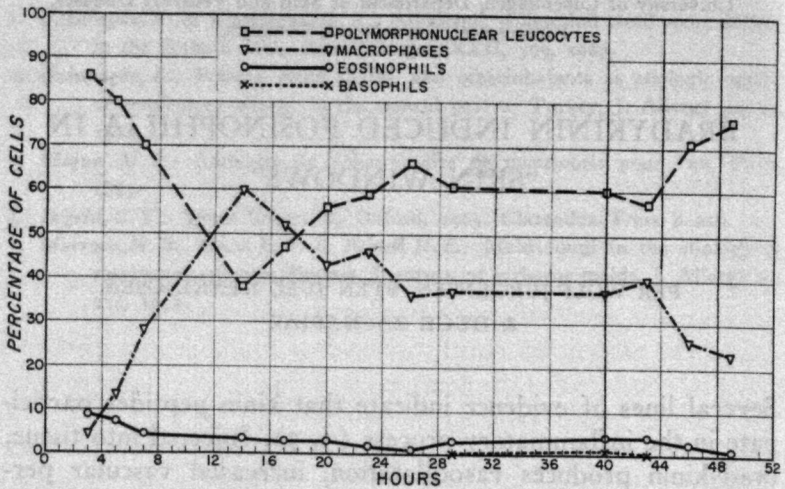


Fig. 1.

Graphic presentation of the cellular sequence in the exudate following intradermal injections of 20 μ g bradykinin beneath the "skin windows". Mean of 11 patients.

patients simultaneously received intradermal injections of 5 mg polymyxin B dissolved in 0.25 ml physiological saline for comparison on the other forearm. Three patients received control injections of 0.2 ml physiological saline. All injections were placed immediately below the excoriations. After removal, the coverslips were dried and stained by the May-Grünwald-Giemsa method. Differential countings were carried out on all preparations.

RESULTS

The cellular exudate in the "skin windows" over the intradermal injections of bradykinin (Fig. 1, 4 and 5) differed strongly from that encountered in the controls with physiological saline (Figs. 3 and 4), while the exudate was similar to that found after intradermal injections of polymyxin B (Figs. 2 and 4). The early phase preparations presented a pronounced eosinophilia. In the ensuing samples the eosinophil counts decreased slowly. The percentage of eosinophils in

SKIN WINDOWS FOLLOWING INJECTION OF POLYMYXIN B

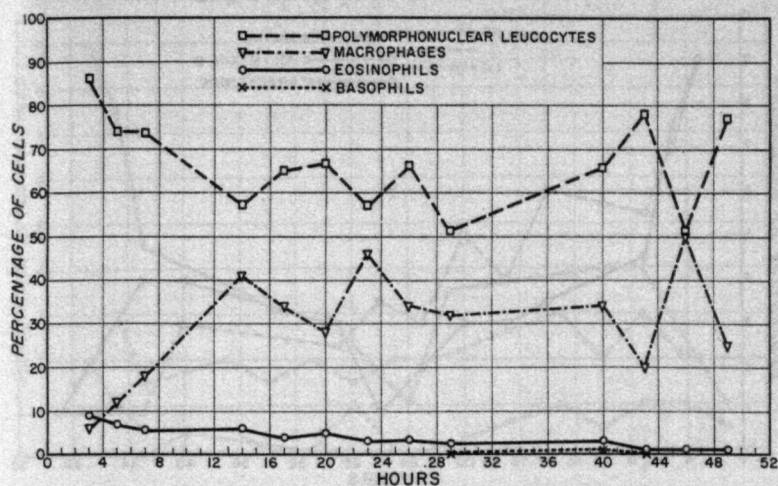


Fig. 2.

The cellular sequence in the exudate following intradermal injections of 5 mg polymyxin B beneath the "skin windows". Mean of 8 patients.

SKIN WINDOWS FOLLOWING INJECTION OF SALINE

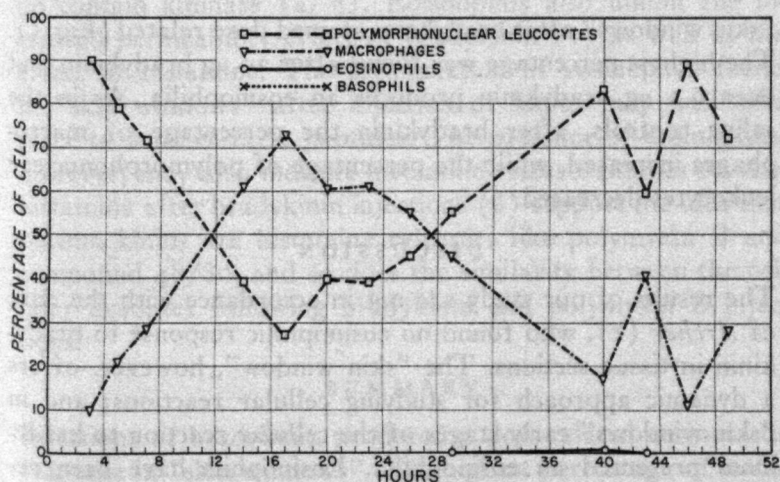


Fig. 3.

The cellular sequence in the exudate following injections of physiological saline beneath the "skin windows". Mean of 3 patients.

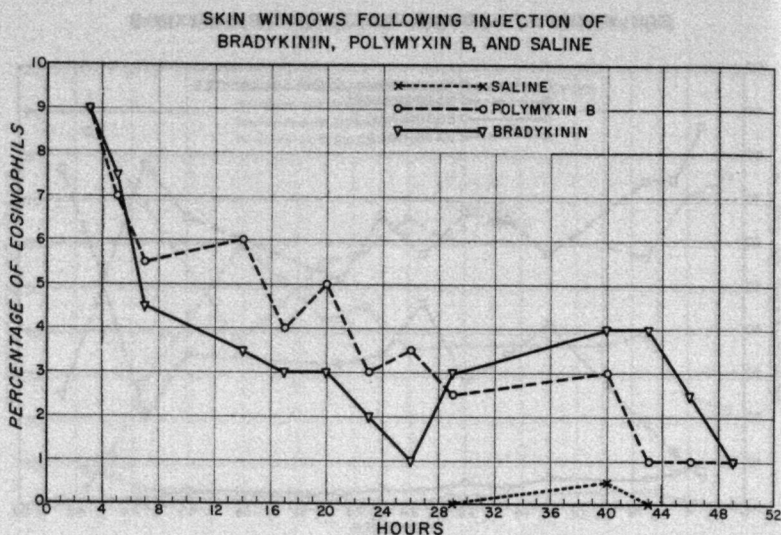


Fig. 4.

Average percentages of eosinophils in "skin windows" following intradermal injections of 20 μ g bradykinin, 5 mg polymyxin B and physiological saline. Mean of 11, 8 and 3 patients.

"skin windows" after bradykinin seemed dose related (Fig. 5). The highest percentage was found after 20 μ g bradykinin, but even 0.1 μ g bradykinin produces an eosinophilia. As in the saline controls, after bradykinin the percentage of macrophages increased, while the percentage of polymorphonuclear leukocytes decreased.

DISCUSSION

The results of our study are not in accordance with the data of Archer (1), who found no eosinophilic response to bradykinin in tissue sections. The "skin window", however, offers a dynamic approach for studying cellular reactions; and in "skin windows" early stages of the cellular reaction to bradykinin presented an eosinophilia. Eosinophils have been regarded as mobile cells capable of inactivating histamine (2). Eosinophils, however, do not contain histaminase, while they

SKIN WINDOWS FOLLOWING INJECTION OF BRADYKININ

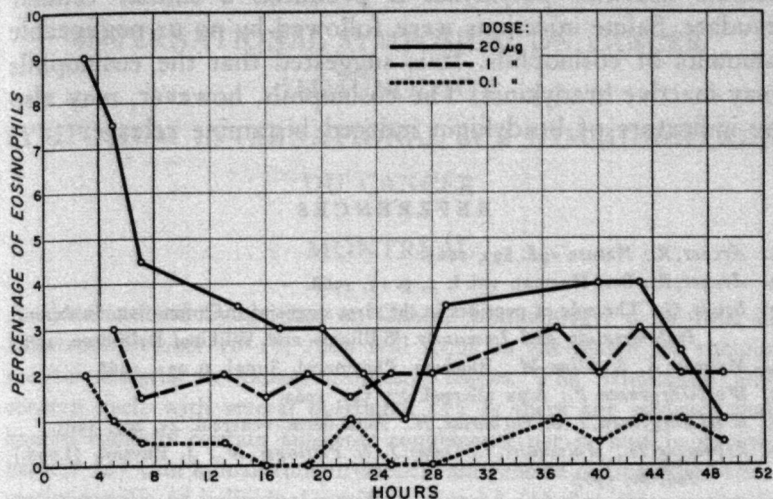


Fig. 5.

Average percentages of eosinophils in "skin windows" following intradermal injections of 20 µg, 1 µg and 0.1 µg bradykinin. Mean of 11, 4 and 4 patients.

do contain kininase (4, 8). Eosinophils also inhibit the increased permeability effect of bradykinin (1) as well as the effect of histamine. The accumulation of eosinophils found in "skin windows" after injection of kinins may well take place to inactive these peptides. The presence of eosinophils, however, may also indicate histamine release. Studies on skin histamine after bradykinin injections (8) support the idea that plasma kinins are histamine releasers like polymyxin B and compound 48/80, and so does the similarity between the cellular exudates following bradykinin and polymyxin B injections.

SUMMARY

Injections of bradykinin produced a dose-related eosinotactic response in "skin windows". The highest percentage of eosinophils was found after injection of 20 µg, but also 0.1 µg bradykinin gave rise to eosinophilia. Injections of the his-

tamine liberator polymyxin B produced a similar cellular exudate. Saline injections were followed by no or negligible amounts of eosinophils. It is suggested that the eosinophils may inactivate bradykinin. The eosinophils, however, may also be indicators of bradykinin induced histamine release.

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